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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,125	10/16/2003	Andrew D. Ellington	CLFR:201USD1	8676

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,125	ELLINGTON ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 12/22/06 to the Office action has been entered. Claims 1-9 are pending.

Election/Restrictions

1. Applicant's election with traverse of Group II, claims 1-19 with the election of raf17-U61C and fluorescein in the reply filed on 12/22/06 is acknowledged. The traversal is on the ground(s) that raf 17, raf17-U61C, raf17-U52C and raf17s have the same target, ATP and are all aptamer in which raf17-U61C, raf17-U52C are all mutant of raf17.

Based upon the reconsideration of the argument, Claims 1-19 are examined with the search of the SEQ ID NO: 17 (raf17), 18 (raf17-U61C) and 19 (raf17s) and all the fluorescent dyes recited in claims 8 and 18.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-19 are vague and indefinite because of the phrases "about equal" and "substantially comprise". It is unclear what is encompassed by the phrases. Clarification is required.

b. Claims 5 and 15 are vague and indefinite because of the phrase "chemically modified nucleotide". It is unclear what is encompassed by the phrases. Clarification is required.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by Winnacker et al. (6,426,409, issued Jul. 30, 2002).

Winnacker et al. disclose a process for the identification and isolation nucleic acid molecules, which are capable of distinguishing a prion protein isoform or peptide fragment or derivative of the prion protein isoform (See column 2, lines 37-41). The nucleic acid used is RNA, modified DNA single stranded or double stranded DNA (See column 3, lines 29-33). The randomized RNA pool M111.1 (See column 7, lines 8-10) is prepared by in vitro transcription from a DNA pool (See column 9, lines 22-24). Randomized sequence is 74 nucleotides (See column 9, lines 42). The RNA aptamer binds specifically to the cellular prion protein isoform (See column 10, lines 49-52). 5' [γ-32P]-ATP labeled or [α-^{32}P] UTP labeled RNA is selected (See column 8, lines 32-64). The ratio of A, C, G, U in RNA (A #1) aptamer in fig. 5 has 18:18:15:32 (A=18, C=15, G=32 and U=18) (See fig. 5 A #1). The fourth nucleotide is uridine (See fig. 5

A#1). It is inherent that the fourth nucleotide is labeled since RNA is [α-^{32}P] UTP labeled RNA (See column 18, lines 32-64).

Since it is unclear what is the definition of the phrase "chemically modified nucleotide", the labeled UTP or ATP is considered to be chemically modified nucleotide.

Since it is unclear what is the definition of the phrase "about equal" and the RNA (A #1) aptamer in fig. 5 has A=18, C=15, G=32 and U=18 (See fig. 5 A #1), the teachings of Winnacker et al. anticipate the limitations of the phrase "about equal" in the amounts of three of four nucleotides.

Winnacker et al. do not explicitly disclose the signaling aptamer having a nucleotide sequence including a random insert of 51 nucleotides. Winnacker et al. disclose that randomized sequence is 74 nucleotides (See column 9, lines 42), which reason on the limitation "the signaling aptamer has a nucleotide sequence including a random insert of 51 nucleotides". Thus, the teachings of Winnacker et al. anticipate the limitations of the claims.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were

made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 6-7, 11-12, 15-17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winnacker et al. (6,426,409, issued Jul. 30, 2002) as applied to claims 1 and 5, and Huizenga et al. (Biochemistry, 1995, Vol. 34, pg. 656-665) in view of Jhaveri et al. (J. Am. Chem. Soc. 2000, Vol.122. pg. 2469-2473).

Huizenga et al. disclose the isolation and characterization of a DNA aptamer that binds to adenosine and ATP in solution (See pg. 656, column 2, second paragraph). The DNA aptamer is made from the synthetic DNA pool via PCR (See pg. 657, column 2, fifth paragraph). ATP-agarose column was used and dATP is labeled (See pg. 657, last paragraph). The DNA is from the random sequence pool (See pg. 658, fig. 2). Huizenga et al. disclose the initial population of single-stranded random-sequence DNA molecules was generated by six cycles of 5' primer extension on a pool of DNA which is PCR amplified dsDNA molecules consisting of 72 random nucleotides flanked by 20 nucleotide prime binding sites (See pg. 658, column 2, last paragraph).

Hunizenga et al. do not disclose that the fourth nucleotide is labeled.

Jhaveri et al. disclose engineering aptamers that contain fluorescent reporters, which include two different anti-adenosine "signaling aptamer", one made from RNA and one made from DNA (See pg. 2469, the Abstract).

Jhaveri et al. do not explicitly disclose that the fourth nucleotide is labeled with fluors. However, Jhaveri et al. indicate that fluorescent dyes were placed adjacent to functional residues and the signaling abilities of the resultant chimeras were evaluated by determining whether changes in fluorescence intensity occurred in the presence of cognate ligand ATP (See pg. 2469, column 2, second paragraph).

One of ordinary skill in the art would have been motivated to apply the teachings of Jhaveri et al. by using fluorescent reporter to design the RNA or DNA signaling aptamers because the signaling aptamer of Jhaveri et al. can be used in generating a wide variety of signaling aptamers for use in sensor arrays (See pg. 2469, the abstract) and Jhaveri et al. indicate that fluorescent dyes were placed adjacent to functional residues and the signaling abilities of the resultant chimeras were evaluated by determining whether changes in fluorescence intensity occurred in the presence of cognate ligand ATP. It would have been prima facie obvious to have the signaling aptamer comprising an RNA nucleotide sequence or DNA nucleotide sequence with labeled fourth nucleotide by fluorescent dye.

8. Claims 3 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winnacker et al. (6,426,409, issued Jul. 30, 2002) or Huizenga et al. (Biochemistry, 1995, Vol. 34, pg. 656-665) in view of Jhaveri et al. (J. Am. Chem. Soc. 2000, Vol.122. pg. 2469-2473) as respectively applied to claims 1 and 5 or claims 6-7, 11-12, 15-17 and 19 above.

The teachings of Winnacker et al. are set forth in section 5 above and the teachings of Huizenga et al. are set forth in section 7 above. None of the references

disclose the specific skewed mole ratio of the random insert of A:C:G:U or A:C:G:T as recited in claims 3 and 14.

However, Winnacker et al. and Huizenga et al. do disclose a randomized sequence of 74 nucleotides in the RNA aptamer of Winnacker et al. (See column 9, lines 42) and the amplified dsDNA molecules consisting of 72 random nucleotides flanked by 20 nucleotide primer binding sites is in the DNA aptamer of Huizenga et al. (See pg. 658, column 2, last paragraph). Since the nucleotide sequence of the aptamer is a random sequence, it is inherent that the ratio of adenine, thymine, uridine, guanine and cytosine is randomized.

One of ordinary skill in the art would have been motivated to optimize the ratio of A:C:G:U in a RNA aptamer or the ratio of A:C:G:T in DNA aptamer for the best binding activity to a target. It would have been prima facie obvious to have the ratios as recited in claims 3 and 14.

9. Claims 8 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Winnacker et al. (6,426,409, issued Jul. 30, 2002) or Huizenga et al. (Biochemistry, 1995, Vol. 34, pg. 656-665) in view of Jhaveri et al. (J. Am. Chem. Soc. 2000, Vol.122. pg. 2469-2473) as respectively applied to claims 1 and 5 or 6-7, 11-12, 15-17 and 19 above, and further in view of Heller (5,849,489, issued Dec. 15, 1998).

The teachings of Winnacker et al. are set forth in section 5 above and the teachings of Huizenga et al. are set forth in section 7 above. None of the references discloses the fluorescent dye recited in claims 8 and 18.

Heller discloses that fluorescein, Texas Red and Rhodamine Green are used as donor chromophores in designing polynucleotide having an acceptor and donor chromophores (See column 6, lines 65-67).

One of ordinary skill in the art would have been motivated to apply these fluorescent dyes in a signaling aptamer because as indicated by Heller et al., target DNA can be quantitatively determined by fluorescent analysis. It would have been prima facie obvious to apply these fluorescent dyes in a signaling aptamer.

10. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Winnacker et al. (6,426,409, issued Jul. 30, 2002) as applied to claims 1 and 5 above, and further in view of Meade et al. (5,591,578, issued Jan. 7, 1997).

The teachings of Winnacker et al. are set forth in section 5 above, Winnacker et al. do not disclose that the fluorescent dye labels a uradine.

Meade et al. disclose the limitations of claim 9 (See column 20, lines 47-50).

One of ordinary skill in the art would have been motivated to apply the fluorescent dye which labels a uradine because as indicated by Meade et al. the method produces complexes which can be used as new class of diagnosis probes (See column 5, lines 39-42) for mismatch detection. It would have been prima facie obvious to attach a fluorescence label to a uradine.

Allowable Subject Matter

11. Claims 2, 4 10, and 13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter:

Concerning claims 2, 4, 10 and 13, no prior art has been found teaching or suggesting SEQ ID NO: 1, 4-7 used as the random insertion in RNA aptamer or DNA aptamer and the signal aptamer is raf17-61C and raf17s.

Summary

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung JT
March 19, 2007

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

3/28/07